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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
| 09/312,351 | 05/14/99 | WOLFF | J MIRUS.006 |

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HM12/0403

| EXAMINER |
|---------------|
| BRUNOVSKIS, P |

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| 1632 | 9 |

DATE MAILED: 04/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/312,351

Applicant(s)

Wolff et al.

Examiner

Peter Brunovskis

Group Art Unit

1632

☒ Responsive to communication(s) filed on Jan 26, 2001

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1035 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-18 is/are pending in the application.

Of the above, claim(s) 1-6 and 15-17 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 7-14 and 18 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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DETAILED ACTION

The Examiner for the instant application has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed in accordance with the instructions at the end of this Action.

The response filed 1/26/01 has been entered. Amendment of claims 7, 8, 12, and 18 is acknowledged. Applicant's arguments filed 1/26/01 will only be considered to the extent that they apply to the pending claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 9-14 are rejected and claims 8 and 18 remain rejected under 35 U.S.C. 112, second paragraph, for the reasons set forth in the Office Action of 9/20/00 and for the reasons set forth below as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 (and dependent claims) is indefinite in its recitation of the limitation "thereby forming two molecules", because it is unclear what "two molecules" the claim is directed to.

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Claim 8 is indefinite in its recitation of a compound comprising a molecule, because it is unclear whether the term compound or molecule are structurally distinguishable in the recited context.

Claim 12 (and dependent claims) is indefinite in its recitation of the phrase “thereby forming two molecules” which lacks antecedent basis and fails to make clear what “two molecules” this limitation is directed to.

Claim 18 remains indefinite because it still lacks antecedent basis. It is unclear what “the disulfide-containing molecule” is directed to, since claim 12 fails to recite any such “molecule”; instead, claim 12 recites “a compound” and a bond capable of forming “two molecules”.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-14 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes “If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).”

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Claims 7-14 and 18 recite compositions or process for making compositions consisting of a compound having “a disulfide bond that is activated by intramolecular attack from a free thiol thereby forming two molecules”. Applicants contend that support for this amendment may be found in the specification on page 19, line 16 and examples 14 and 38. Page 19, line 16 does not mention or inference concerning a process “forming two molecules”, but rather describes a cleavable disulfide bond wherein “a chemical bond between atoms is broken”. This type of cleavage is not limited to bonds resulting in formation of two molecules, but embraces cleavable intramolecular bonds that preclude formation of “two molecules”. Examples 14 and 38 describe “form[ation] of two molecules” only in the context of *particular compositions*. There is no evidence of record that Applicants contemplated this limitation in the broader context of the generic compositions recited in claims 7-14 or 18 to which the limitation is directed, nor is there any established nexus between the two, particularly since the nature of the “two molecules” is not readily apparent from reading the claims and since the specification fails to provide a nexus between the generic embodiments recited and the formation of two molecules including those comprising e.g. the range of generic polymers or generic ligand groups as recited in claims 10 and 14. A single species does not provide written description or evidence for possession for any and all arbitrary genera into which, in hindsight, it may fall.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7-14 and 18 remain rejected under 35 U.S.C. 102(b) for the reasons set forth in the Office Action of 9/20/00 and for the reasons set forth below as being anticipated by Wagner et al. (Proc. Nat. Acad. Sci. USA 87(9):3410-3414, 5/1990), as evidenced by MacGillivray et al. (Proc. Nat. Acad. Sci. USA 79(8):2504-2508, 4/1982).

Applicant's arguments filed 1/26/01 have been fully considered but they are not persuasive. As stated in the Office Action of 9/20/00, the specification states that "cystine is reduced 3-15 times faster than oxidized glutathione" (p. 2, lines 30-31). Thus the intramolecular bonds in the compositions of Wagner meet the limitations of part (a) of claims 7 and 12; consequently, the rest of the arguments concerning acylation of cysteine amino groups and their resultant pKa values are moot. Nevertheless, it is unclear what basis Applicants rely upon to assert that e.g. "A thiol of transferrin has a pKa 0.6 greater than the thiols formed by Applicants' process" or that "Wagner et al. describes thiol pKa's that are the same as glutathione".

Claims 7-14 and 18 remain rejected under 35 U.S.C. 102(b) for the reasons set forth in the Office Action of 9/20/00 and for the reasons set forth below as being anticipated by Stassen et al.

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(Thrombosis and Haemostasis 74(2):646-654, 8/1995), as evidenced by Elliott et al. (J. Pharm. Exp. Therapeut. 273(1):280-284, 4/1995) and Voet (In Biochemistry, Second Edition, John Wiley and Sons, Publishers, 1995).

Applicant's arguments filed 1/26/01 have been fully considered but they are not persuasive. Applicants amendment does not obviate the rejection, since the claims are not limited to embodiments having "a disulfide bond that is activated by intramolecular attack from a free thiol thereby forming two molecules", but rather recite a Markush group containing a compound having a disulfide bond that is cleaved more rapidly than oxidized glutathione or having a lower pKa than glutathione as described in the Office Action of 9/20/00.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 7-14 and 18 remain rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) for the reasons set forth in the Office Action of 9/20/00 and for the reasons set forth below as obvious over Wagner et al. (Proc. Nat. Acad. Sci. USA 87(9):3410-3414, 5/1990), as evidenced by Lodish et al. (J. Biol. Chem. 266(23):14835-14838, 8/1991).

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Applicant's arguments filed 1/26/00 have been fully considered but they are not persuasive, since they merely assert that amendment of claims 7 and 12 obviates the §103 rejection without explaining how. Applicant are reminded of the arguments to Applicants response as directed to "thereby forming two molecules" which does not cover the full scope of the claimed subject matter.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

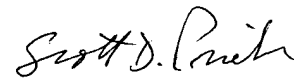
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Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Brunovskis whose telephone number is (703) 305-2471. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda can be reached at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Patent Analyst, Patsy Zimmerman whose telephone number is (703) 308-8338.

Peter Brunovskis, Ph.D.
Patent Examiner
Art Unit 1632



SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER